This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1-43. (canceled)

44. (currently amended) A method of treating an organism having a disease characterized by the undesired production of a protein comprising contacting the organism with a compound comprising a plurality of units linked by covalent linkages in a sequence that is hybridizable to a complementary nucleic acid encoding the protein, wherein:

said units are selected from nucleosides and nucleobases:

said nucleosides are selected from α-nucleosides, ß-nucleosides including 2'-deoxy-erythro-pentofuranosyl ß-nucleosides, 4'-thionucleosides, and carbocyclic-nucleosides;

said nucleobases are selected from purin-9-yl and pyrimidin-1-yl heterocyclic bases;

said linkages are selected from charged 3'-5' phosphorous, neutral 3'-5' phosphorous, charged 2'-5' phosphorous, neutral 2'-5' phosphorous or non-phosphorous linkages; and

said sequence of linked units is divided into at least two regions, wherein:

a first of said regions includes said nucleobases linked by non-phosphorous linkages and nucleobases that are attached to phosphate linkages via non-sugar tethering groups, and nucleosides selected from said α-nucleosides linked by charged and neutral 3'-5' phosphorous linkages, said α-nucleosides linked by charged and neutral 2'-5' phosphorous linkages, said α-nucleosides linked by non-phosphorous linkages, said 4'-thionucleosides linked by charged and neutral 3'-5' phosphorous linkages, said 4'-thio-nucleosides linked by charged and neutral 2'-5' phosphorous linkages, said 4'-thionucleosides linked by non-phosphorous linkages, said carbocyclic-nucleosides linked by charged and neutral 3'-5' phosphorous linkages, said carbocyclic-nucleosides linked by charged and neutral 2'-5' phosphorous linkages, said carbocyclic-nucleosides linked by non-phosphorous linkages,

said ß-nucleosides linked by charged and neutral 2'-5' linkages, and said ß-nucleosides linked by non-phosphorous linkages; and

a second of said regions includes said 2'-deoxy-erythro-pentofuranosyl ß-nucleosides linked by charged 3'-5' phosphorous linkages having a negative charge at physiological pH

wherein the compound interferes with production of the protein.

45. (canceled)

46. (canceled)

47. (currently amended) A method of treating an organism having a disease characterized by the undesired production of a protein comprising contacting the organism with a compound of comprising a plurality of units linked by covalent linkages in a sequence that is hybridizable to a complementary nucleic acid encoding the protein, wherein:

said units are selected from nucleosides and nucleobases;

said nucleosides are selected from α-nucleosides, ß-nucleosides, 4'-thionucleosides and carbocyclic-nucleosides;

said nucleobases are selected from purin-9-yl and pyrimidin-1-yl heterocyclic bases;

said linkages are selected from charged phosphorous, neutral phosphorous or non-phosphorous linkages; and

said sequence of linked units is divided into at least two regions, wherein:

a first of said regions includes said α-nucleosides linked by charged and neutral 3'-5' phosphorous linkages, said α-nucleosides linked by charged and neutral 2'-5' phosphorous linkages, said α-nucleosides linked by non-phosphorous linkages, said 4'-thionucleosides linked by charged and neutral 3'-5' phosphorous linkages, said 4'-thionucleosides linked by charged and neutral 2'-5' phosphorous linkages, said 4'-thionucleosides linked by non-phosphorous linkages, said carbocyclic-nucleosides linked by charged and neutral phosphorous linkages, said carbocyclic-nucleosides linked by non-

phosphorous linkages, said ß-nucleosides linked by charged and neutral 3'-5' linkages, said ß-nucleosides linked by charged and neutral 2'-5' linkages, and said ß-nucleosides linked by non-phosphorous linkages; and

a second of said regions including said nucleobases linked by non-phosphorous linkages and nucleobases that are attached to phosphate linkages via a non-sugar tethering moiety

wherein the compound interferes with production of the protein.

48. (canceled).

49. (currently amended) A method of treating an organism having a disease characterized by the undesired production of a protein comprising contacting said organism with an oligonucleotide having a sequence of nucleotides capable of specifically hybridizing to a strand of ribonucleic acid coding for said protein, where at least one of said nucleotides is functionalized to increase nuclease resistance of the oligonucleotide, where a plurality of the nucleotides have a substituent group located thereon to increase binding affinity of the oligonucleotide to a complementary strand of sequence-specific ribonucleic acid, and where a plurality of the nucleotides have 2'-deoxy-erythro-pentofuranosyl sugar moieties, wherein the compound interferes with production of the protein.

50. (previously presented) The method of claim 49 wherein said substituent group for increasing binding affinity comprises a 2'-substituent group.

51. (previously presented) The method of claim 49 wherein said substituent group for increasing binding affinity comprises a 2'-substituent group that is fluoro, C1-C9 alkoxy, C1-C9 aminoalkoxy, allyloxy, imidazolealkoxy or poly(ethylene glycol).

52. (previously presented) The method of claim 49 wherein each of said nucleotides is a phosphorothioate or phosphorodithioate nucleotide.

53. (previously presented) The method of claim 49 wherein the 3' terminal nucleotide of said oligonucleotide includes a nuclease resistance modifying group on at least one of the 2' or the 3' positions of said nucleotide.

54. (previously presented) The method of claim 49 wherein:

a plurality of said nucleotides bear substituent groups that increases binding affinity of said oligonucleotide to said sequence-specific ribonucleic acid, said substituent-bearing nucleotides being divided into a first nucleotide unit sub-sequence and a second nucleotide unit sub-sequence; and

said plurality of 2'-deoxy-erythro-pentofuranosyl nucleotides is positioned in said sequence of nucleotides between said first nucleotide unit sub-sequence and said second nucleotide unit sub-sequence.

55. (previously presented) The method of claim 49 wherein:

a plurality of said nucleotides bear substituent groups that increase binding affinity of said oligonucleotide to said complementary strand of nucleic acid; and

at least a portion of said substituent-bearing nucleotides are consecutively located at one of the 3' terminus or the 5' terminus of said oligonucleotide.

56. (previously presented) The method of claim 49 wherein at least five of said nucleotides have 2'-deoxy-erythro-pentofuranosyl sugar moieties, said at least five 2'-deoxy-erythro-pentofuranosyl nucleotides being consecutively located in said sequence of nucleotides.

57. (previously presented) The method of claim 49 wherein from one to about eight of said nucleotides bear a substituent group that increases the binding affinity of said oligonucleotide to said complementary strand, said substituent-bearing nucleotides being consecutively located in said sequence of nucleotides.

58. (previously presented) The method of claim 49 wherein:

from one to about eight of said nucleotides bear a substituent group for increasing the binding affinity of said oligonucleotide to said complementary strand, said substituent-bearing nucleotides being consecutively located in said sequence of nucleotides; and

at least five of said nucleotides have 2'-deoxy-erythro-pentofuranosyl sugar moieties, said at least five 2'-deoxy-erythro-pentofuranosyl nucleotides being consecutively located in said sequence of nucleotides.

59. (currently amended) A method of concurrently enhancing hybridization and RNase H activation in an organism comprising contacting the organism with an oligonucleotide having a sequence of nucleotides capable of specifically hybridizing to a sequence-specific ribonucleic acid where at least one of said nucleotides is functionalized to increase nuclease resistance of the oligonucleotide, where a plurality of the nucleotides have a substituent group located thereon to increase binding affinity of the oligonucleotide to a complementary strand of sequence-specific ribonucleic acid, and where a plurality of the nucleotides have 2'-deoxy-erythro-pentofuranosyl sugar moieties, wherein hybridization of the oligonucleotide to the sequence-specific ribonucleic acid and concomitant RNase H activation is enhanced.

60. (previously presented) The method of claim 59 wherein said substituent group for increasing binding affinity comprises a 2'-substituent group.

61. (previously presented) The method of claim 59 wherein said substituent group for increasing binding affinity comprises a 2'-substituent group that is fluoro, C1-C9 alkoxy, C1-C9 aminoalkoxy, allyloxy, imidazolealkoxy or poly(ethylene glycol).

62. (previously presented) The method of claim 59 wherein each of said nucleotides is a phosphorothioate or phosphorodithioate nucleotide.

63. (previously presented) The method of claim 59 wherein the 3' terminal nucleotide of said oligonucleotide includes a nuclease resistance modifying group on at least one of the 2' or the 3' positions of said nucleotide.

64. (previously presented) The method of claim 59 wherein:

a plurality of said nucleotides bear substituent groups that increases binding affinity of said oligonucleotide to said sequence-specific ribonucleic acid, said substituent-bearing nucleotides being divided into a first nucleotide unit sub-sequence and a second nucleotide unit sub-sequence; and

said plurality of 2'-deoxy-erythro-pentofuranosyl nucleotides is positioned in said sequence of nucleotides between said first nucleotide unit sub-sequence and said second nucleotide unit sub-sequence.

65. (previously presented) The method of claim 59 wherein:

a plurality of said nucleotides bear substituent groups that increase binding affinity of said oligonucleotide to said complementary strand of nucleic acid; and

at least a portion of said substituent-bearing nucleotides are consecutively located at one of the 3' terminus or the 5' terminus of said oligonucleotide.

66. (previously presented) The method of claim 59 wherein at least five of said nucleotides have 2'-deoxy-erythro-pentofuranosyl sugar moieties, said at least five 2'-deoxy-erythro-pentofuranosyl nucleotides being consecutively located in said sequence of nucleotides.

67. (previously presented) The method of claim 59 wherein from one to about eight of said nucleotides bear a substituent group that increases the binding affinity of said oligonucleotide to said complementary strand, said substituent-bearing nucleotides being consecutively located in said sequence of nucleotides.

68. (previously presented) The method of claim 59 wherein:

from one to about eight of said nucleotides bear a substituent group for increasing the binding affinity of said oligonucleotide to said complementary strand, said substituent-bearing nucleotides being consecutively located in said sequence of nucleotides; and

at least five of said nucleotides have 2'-deoxy-erythro-pentofuranosyl sugar moieties, said at least five 2'-deoxy-erythro-pentofuranosyl nucleotides being consecutively located in said sequence of nucleotides.